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NOTICE OF ALLOWANCE AND FEE(S) DUE

23859

7590

12/31/2008

Ballard Spahr Andrews & Ingersoll, LLP SUITE 1000 999 PEACHTREE STREET ATLANTA, GA 30309-3915 EXAMINER

NOAKES, SUZANNE MARIE

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 12/31/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,027	08/04/2003	Artem Gennady Evdokimov	01279.0009U1	5050

TITLE OF INVENTION: THREE DIMENSIONAL COORDINATES OF HPTPBETA

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1510	\$300	\$0	\$1810	03/31/2009

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

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If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

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III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

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ATLANTA, GA	30309-3915			(Depositor's name)				
							(Signature)	
							(Date)	
APPLICATION NO.	FILING DATE		FIRST NAMED INVENTO	₹	ATTOR	RNEY DOCKET NO.	CONFIRMATION NO.	
10/634,027	08/04/2003	•	Artem Gennady Evdokim	ov	0	1279.0009U1	5050	
TITLE OF INVENTION	: THREE DIMENSION	AL COORDINATES OF	НРТРВЕТА					
APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSU	E FEE	TOTAL FEE(S) DUE	DATE DUE	
nonprovisional	NO	\$1510	\$300	\$0		\$1810	03/31/2009	
EXAM	IINER	ART UNIT	CLASS-SUBCLASS]				
NOAKES, SUZ	ZANNE MARIE	1656	435-195000	_				
1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363). ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached. ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.			(1) the names of up t or agents OR, alternat (2) the name of a sing registered attorney or 2 registered patent att	For printing on the patent front page, list the names of up to 3 registered patent attorneys agents OR, alternatively, the name of a single firm (having as a member a gistered attorney or agent) and the names of up to registered patent attorneys or agents. If no name is led, no name will be printed.				
PLEASE NOTE: Un	less an assignee is ident th in 37 CFR 3.11. Comp	ified below, no assignee	THE PATENT (print or ty data will appear on the T a substitute for filing ar (B) RESIDENCE: (CIT	patent. If an assign assignment.			cument has been filed for	
Please check the appropr	riate assignee category or	categories (will not be pr	rinted on the patent):	Individual 🖵 C	orporatio	on or other private grou	p entity Government	
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5. Change in Entity Sta	,	· · · · · · · · · · · · · · · · · · ·						
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interest as shown by the	records of the United Sta	ites Patent and Trademark	of from anyone other than of Office.	ше аррисант; а гед	istered a	tiorney of agent; of the	assignee of other party in	
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10/634,027 08/04/2003		Artem Gennady Evdokimov	01279.0009U1 5050	
23859 7.	590 12/31/2008		EXAM	INER
Ballard Spahr Ai	ndrews & Ingersoll, I	NOAKES, SUZANNE MARIE		
SUITE 1000			ART UNIT	PAPER NUMBER
999 PEACHTREE ATLANTA, GA 3			1656 DATE MAILED: 12/31/200	8

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 193 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 193 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 (571)-272-4200.

	Application No.	Applicant(s)					
	10/624 027	EVDOKIMOV ET AL.					
Notice of Allowability	10/634,027 Examiner	Art Unit					
	OUZANNE M NOAKEO	1050					
	SUZANNE M. NOAKES	1656					
The MAILING DATE of this communication appear All claims being allowable, PROSECUTION ON THE MERITS IS herewith (or previously mailed), a Notice of Allowance (PTOL-85) NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIOF of the Office or upon petition by the applicant. See 37 CFR 1.313	(OR REMAINS) CLOSED in this a or other appropriate communication IGHTS. This application is subject	application. If not included on will be mailed in due course. THIS					
1. \boxtimes This communication is responsive to <u>the amendments filed</u>	l 16 September 2008 and the agre	eed upon Examiner's amendments.					
2. The allowed claim(s) is/are 26-33 and 35.							
 3. ☐ Acknowledgment is made of a claim for foreign priority ur a) ☐ All b) ☐ Some* c) ☐ None of the: 1. ☐ Certified copies of the priority documents have 2. ☐ Certified copies of the priority documents have 	e been received.						
Copies of the certified copies of the priority does	• •						
International Bureau (PCT Rule 17.2(a)).	odinente nave been received in thi	o haterial stage application from the					
* Certified copies not received:							
Applicant has THREE MONTHS FROM THE "MAILING DATE" noted below. Failure to timely comply will result in ABANDONN THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.		ly complying with the requirements					
4. A SUBSTITUTE OATH OR DECLARATION must be subm INFORMAL PATENT APPLICATION (PTO-152) which give							
5. CORRECTED DRAWINGS (as "replacement sheets") mus	st be submitted.						
(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached							
1) hereto or 2) to Paper No./Mail Date							
(b) ☐ including changes required by the attached Examiner's Paper No./Mail Date	(b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date						
Identifying indicia such as the application number (see 37 CFR 1 each sheet. Replacement sheet(s) should be labeled as such in t							
6. DEPOSIT OF and/or INFORMATION about the depo attached Examiner's comment regarding REQUIREMENT							
Attachment(s)							
1. Notice of References Cited (PTO-892)	5. Notice of Informal	• •					
2. Notice of Draftperson's Patent Drawing Review (PTO-948)	6. ☐ Interview Summa Paper No./Mail D						
3. Information Disclosure Statements (PTO/SB/08),	7. 🛛 Examiner's Amen	dment/Comment					
Paper No./Mail Date 4.	8. 🛛 Examiner's Stater	ment of Reasons for Allowance					
	9. 🔲 Other						
SUZANNE M. NOAKES							
Primary Examiner							
Art Unit: 1656							

Art Unit: 1656

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Richard Echler on 12 December 2008.

The application has been amended as follows:

In the claims:

CANCEL Claims 10-24.

- 25. (Currently Amended) A method of identifying a drug candidate compound for the treatment of an angiogenic mediated disorder, comprising:
 - a) employing the three-dimensional structural coordinates of the human <u>protein tyrosine phosphatase beta</u> (HPTPbeta) catalytic domain [SEQ ID NO:7] as set forth in Figures 202-252 to graphically image the HPTPbeta catalytic domain [SEQ ID NO:7], and determining the binding mode of a compound within the catalytic domain;
 - b) selecting one or more compounds which have similar binding modes the best fit with the HPTPbeta catalytic domain [SEQ ID NO:7] as set forth in Figures 202-252 wherein the compounds are computationally positioned at one or more areas of said imaged HPTPbeta catalytic domain [SEQ ID NO:7] and
 - c) assaying analyzing the ability of said drug candidate compound to bind or modulate HPTPbeta activity.
- 26. (Currently Amended) A method of identifying a drug candidate compound for the treatment of an angiogenic mediated disorder, comprising:
 - a) employing the three-dimensional structural coordinates of the HPTPbeta catalytic domain [SEQ ID NO:7] as set forth in Figures 7-102 to graphically image the HPTPbeta catalytic domain [SEQ ID NO:7], and determining the binding

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mode of a compound within the catalytic domain;

b) selecting one or more compounds which have similar binding modes the best fit with the HPTPbeta catalytic domain [SEQ ID NO:7] as set forth in Figures 7-102 wherein the compounds are computationally positioned positioning a drug candidato compound at one or more areas of said imaged HPTPbeta catalytic domain [SEQ ID NO:7]; and

- c) assaying the ability of said drug candidate compound to bind or modulate HPTPbeta activity.
- 27. (Previously Presented) The method according to claim 25, wherein said drug candidate compound is positioned at at least amino acid residues 152, 74-77, 209-214, 244-253, 288-290, and 293 of [SEQ ID NO:7].
- 28. (Previously Presented) The method according to claim 26, wherein said drug candidate compound is positioned at at least amino acid residues 152, 74-77, 209-214, 244-253, 288-290, and 293 of [SEQ ID NO:7].
- 29. (Previously Presented) The method according to claim 25, wherein said drug candidate compound is positioned at at least amino acid residues 76-80, 48-66, 284-292 and 212-214 of [SEQ ID NO:7].
- 30. (Previously Presented) The method according to claim 26, wherein said drug candidate compound is positioned at at least amino acid residues 76-80, 48-66, 284-292 and 212- 214 of [SEQ ID NO:7].
- 31. (Previously Presented) The method according to claim 25, wherein said drug candidate compound is positioned at at least amino acid residues 69-76, 119-123, and 149-154 of [SEQ ID NO:7].
- 32. (Previously Presented) The method according to claim 26, wherein said drug candidate compound is positioned at at least amino acid residues 69-76, 119-123, and 149-154 of [SEQ ID NO:7].
- 33. (Currently Amended) A method of identifying an inhibitor of an HPTPbeta molecule, comprising:
 - a) providing a crystal of HPTPbeta comprising the amino acid residues of SEQ ID NO:7 which either has space group P2₁2₁2₁ and unit cell parameters a=39Å, b=

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72Å, c=120 Å and $\alpha=\beta=\gamma=90^\circ$, or space group P2₁ with unit cell parameters of a=62Å, b=70Å, c=70Å and $\alpha=90^\circ$, $\beta=93^\circ$, $\gamma=90^\circ$;

- b) subjecting the crystal in (a) to X-ray diffraction and determining the threedimensional structure coordinates of the HPTPbeta catalytic domain;
- c) employing the three-dimensional structure coordinates from (b) to graphically display the three-dimensional structure and identifying the active binding site residues of Asn74 Asn75 Ile76, Leu77, Cys152, Pro209, Asp210, His211, Gly212, Va1213, Pro214, Cys244, Ser245, Ala246, Gly247, Va1248, Gly249, Arg250, Thr251, Gly252, Thr253, Gln288, Thr289, Glu290, and Tyr293;
- b) determining the three-dimensional atomic coordinates of amino acids Asn74 Asn75 Ile76, Leu77, Cys152, Pro209, Asp210, His211, Gly212, Va1213, Pro214, Cys244, Ser245, Ala246, Gly247, Va1248, Gly249, Arg250, Thr251, Gly252, Thr253, Gln288, Thr289, Glu290, and Tyr293 of an active binding site of the HPTPbeta molecule by X-ray diffraction of the crystal;
- [[e]] d) using the atomic coordinates of amino acids Asn74 Asn75 Ile76, Leu77, Cys 152, Pro209, Asp210, His211, Gly212, Va1213, Pro214, Cys244, Ser245, Ala246, Gly247, Va1248, Gly249, Arg250, Thr251, Gly252, Thr253, Gln288, Thr289, Glu290, and Tyr293 as determined in c) to generate a three-dimensional structure of a molecule comprising an HPTPbeta active site binding pocket so that the root mean square deviation of conserved residue backbone atoms is less than 1.5 Å as compared to the three-dimensional coordinates in a-c), to generate a three-dimensional structure of a molecule comprising an HPTPbeta active site binding pocket;
- [[d]]) e) employing the three-dimensional structure from d) to design or select a potential drug candidate; and
- [[e]]) <u>f</u>) contacting the potential drug candidate with the molecule to determine the ability of the potential inhibitor to associate with the molecule.

34. CANCEL

- 35. (Currently Amended) A method of identifying an inhibitor of an HPTPbeta molecule, comprising:
 - a) providing a crystal of HPTPbeta comprising the amino acid residues of SEQ ID NO:7 which either has space group P2₁2₁2₁ and unit cell parameters a=39Å, b=

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72Å, c=120 Å and $\alpha=\beta=\gamma=90^\circ$, or space group P2₁ with unit cell parameters of a=62Å, b=70Å, c=70Å and $\alpha=90^\circ$, $\beta=93^\circ$, $\gamma=90^\circ$;

- b) subjecting the crystal in (a) to X-ray diffraction and determining the three-dimensional structure coordinates of the HPTPbeta catalytic domain;
- c) employing the three-dimensional structure coordinates from (b) to graphically display the three-dimensional structure and identifying the active binding site residues of Glu48, Glu49, Leu50, Lys51, Asp52, Va153, Gly54, Arg55, Asn56, Gln57, Ser58, Cys59, Asp60, Ile61, Ala62, Leu63, Leu64, Pro65, Glu66, Ile76, Leu77, Pro78, Tyr79, Asp80, Gly212, Va1213, Pro214, Va1284, His285, Met286, Va1287, Gln288, Thr289, Glu290, Cys291, and Gln292;
- b) determining the three-dimensional atomic coordinates of amino acids Glu48, Glu49, Leu50, Lys51, Asp52, Va153, Gly54, Arg55, Asn56, Gln57, Ser58, Cys59, Asp60, Ile61, Ala62, Leu63, Leu64, Pro65, Glu66, Ile76, Leu77, Pro78, Tyr79, Asp80, Gly212, Va1213, Pro214, Va1284, His285, Met286, Va1287, Gln288, Thr289, Glu290, Cys291, and Gln292 of an active binding site of the HPTPbeta molecule by X-ray diffraction of the crystal;

[[e]]) d) using the atomic coordinates of amino acids Glu48, Glu49, Leu50, Lys51, Asp52, Va153, Gly54, Arg55, Asn56, Gln57, Ser58, Cys59, Asp60, Ile61, Ala62, Leu63, Leu64, Pro65, Glu66, Ile76, Leu77, Pro78, Tyr79, Asp80, Gly212, Va1213, Pro214, Va1284, His285, Met286, Va1287, Gln288, Thr289, Glu290, Cys291, and Gln292 as determined in c) to generate a three-dimensional structure of a molecule comprising an HPTPbeta active site binding pocket so that the root mean square deviation of conserved residue backbone atoms is less than 1.5 Å as compared to the three-dimensional coordinates in a-c), to generate a three-dimensional structure of a molecule comprising an HPTPbeta active site binding pocket;

- [[d]]) e) employing the three-dimensional structure from d) to design or select a potential drug candidate; and
- [[e]]) f) contacting the potential drug candidate with the molecule to determine the ability of the potential inhibitor to associate with the molecule.

36. CANCEL.

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Reasons for Allowance

2. The following is an examiner's statement of reasons for allowance: The claims are drawn to methods of identifying candidate drug compounds that bind to the catalytic domain of the human protein tyrosine phosphatase beta (HPTPbeta). The method utilizes in silico screening of candidate compounds by emplying the three-dimensional structure of the catalytic domain of said HPTPbeta (SEQ ID NO: 7), which has been characterized by as two different three-dimensional structures (e.g. Figures 7-102 and Figures 202-252) both of which are apo-structures, wherein the former (Figures 7-102) is derived from monoclinic crystals, the later derived from othorhrombic crystals (Figures 202-252). The three-dimensional structures and specifically the noted and identified binding pocket residues as limited in the claims are not taught in the prior art nor are they obvious over the prior art. While the main focus in the prior art has centered around the well known human protein tyrosine phosphatase 1B protein, little is known about the catalytic binding pocket of the HPTPbeta enzyme. Thus, utilizing the structural coordinates as outlined in claims 25, 26, 33 and 35 are both novel and nonobvious over the art of record. Thus, claims 26-33 and 35 are allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

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3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SUZANNE M. NOAKES/ Primary Examiner, Art Unit 1656 12 December 2008